Further Applicants would like to file a Request for Continued Examination (RCE) in response to the June 1, 2004 Advisory Action in compliance with 37 CFR 1.114 and respectfully request the fee of THREE HUNDRED EIGHTY FIVE DOLLARS ($385) be charged to Deposit Account 50-1891.

Amendments:

Please enter the Amendment filed on April 1, 2004.

REMARKS

Claims 38-76 are pending in this application.

Amendment Rejections - 37 CFR 1.113

The Examiner stated that the proposed amendment(s) will not be entered because they raise new issues that would require further consideration and/or search. The Examiner further stated that Applicant has amended claim 38 to include a particle-size distribution that is about the same or less than the polymeric bone-cement's component's particle size distribution. The issues discussed in the previous office actions are all drawn to "about the same" particle size distribution. The addition of "or less than" presents a new issue that would require further search and consideration.

In response but without conceding the correctness of the Examiner's position and to expedite the prosecution of this application, Applicants have requested a Request for Continued Examination (RCE) for entry of the Amendment. Therefore the "new issue" in the Amendment should be entered and considered.

Exhibits Rejection

At item number 5 of the Advisory Action, the Examiner stated the Exhibits have been considered but do NOT place the application in condition for allowance because whether the larger particles rise up (as in the exhibits) or fall to the bottom (as in Remington) they still both underscore the fact that it would have been obvious to incorporate particles of about the same size to prevent demixing.

In response, Applicants respectfully traverse the above ground of rejection. Applicants' claimed invention recites: A composition useful as local drug delivery system comprising: (a) a polymeric bone-cement component in the form of particles, and (b) an anti-resorptive agent in the form of particles, wherein the anti-resorptive agent's particle-size distribution is about the same or less than the polymeric bone-cement component's particle-size distribution.

Applicants maintain that Remington is irrelevant to the Applicants' claimed invention. The particle size issue that Remington's article addresses relates to the blending of separate powder components of a formulation to ensure uniformity and minimize demixing. Applicants would note that, on settling larger particles tend to rise to the surface, the opposite of what Remington's article states.

However, Applicants' claimed invention is to ensure that the composition would be useful as a local drug delivery system. The claimed invention provides that particle distribution within the POLYMERIZED material placed against the bone will maximize the quantity of drug positioned against the bone and significantly improve the uniformity of drug delivery to bone adjacent to the polymerized cement. In addition, smaller sized particles will minimize the potential of local high concentration of drug delivered to adjacent bone that may have

adverse physiologic effects. Regardless of the particle size, blending uniformity is accomplished during powder formulation and again during the mixing of the powder formulation with the catalyst prior to clinical use. It is the particle size of the drug that will ensure maximum exposure of the drug to the adjacent bone in the polymerized cement.

Further, drug formulated within PMMA cement is only delivered to bone from those particles that exist within the first ten (10) microns of the PMMA cement adjacent to bone. There is no diffusion of drug from inner regions of the PMMA because the PMMA polymerized matrix is impermeable to water and the matrix is a closed pore system. Thus, drug distribution is only from drug particles that are released from the surface between bone and cement. The bulk of the drug, over 99 percent remains trapped within the matrix. Thus, the surface distribution of particles is most essential to the uniformity of drug delivery to bone. The smaller the particles the more of them distributed around the surface of the cement-bone surface. Applicants attach hereto as **Exhibit** 1 a diagram detailing particle size in relationship to drug delivery uniformity.

Remington addresses the issue of mixing, i.e. the uniformity of drug within powder during blending prior to packaging (gram drug/gram blend). Nothing in Remington teaches the importance of maximization of drug positioned against the bone. Accordingly, Remington is irrelevant to the claimed invention.

Further, another aspect of the invention which recites: a composition comprising: (a) a bone-cement selected from the group consisting of (1) an organic cement, (2) an inorganic cement, and (3) a composite cement; and (b) an anti-resorptive amount of an anti-resorptive agent wherein the anti-resorptive agent is present in an amount that does not compromise the cement's chemical or mechanical properties but sufficient to

prevent loosening of the bone cement from the living bone should be allowable since Remington is also irrelevant.

Conclusion

Applicants believe that the above arguments address all issues raised in the June 1, 2004 Advisory Action and respectfully request the reconsideration and withdrawal of all ground of rejections pending in this application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

No fee other than the $420 for the second and third month extension of time and $385.00 Request for Continued Examination (RCE) fee is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 50-1891.

Respectfully submitted,
Albert Wai-Kit Chan

Albert Wai-Kit Chan
Registration No. 36,479
Attorney for Applicants
Law Offices of
Albert Wai-Kit Chan, LLC
World Plaza, Suite 604
141-07 20th Avenue
Whitestone, New York 11357
Tel: (718) 357-8836
Fax: (718) 357-8615
E-mail: kitchanlaw@aol.com